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HFD-613

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19425/S-019 **AUG 13 1998**

GlaxoWellcome
Attention: Ms. Elizabeth A. Nies
Five Moore Drive
Research Triangle Park, NC 27709

Dear Ms. Nies:

Please refer to your supplemental new drug application dated July 17, 1998, received July 20, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Trandate (labetalol hydrochloride) 5 mglmL Injection.

We acknowledge receipt of your submission dated July 17. 1998.

We note that this supplement was submitted as a 'Special Supplement-Changes Being Effected' under 21 CFR 314.70(c).

This supplemental new drug application provides for final printed labeling revised as follows:

1. The following sentence has been added to the WARNINGS/Major Surgery subsection:

   Several deaths have occurred when Trandate (labetalol HCI) Injection was used during surgery (including when used in cases to control bleeding).

2. The following statement has been added to the CONTRAINDICATIONS section:

   Beta-blockers, even those with apparent cardioselectivity, should not be used in patients with a history of obstructive airway disease, including asthma.

3. The WARNINGS/Rapid Decrease of Blood Pressure subsection has been changed to read as follows:

   A number of adverse reactions, including cerebral infarction, optic nerve infarction, angina, and ischemic changes in the electrocardiogram, have been reported with other agents when severely elevated blood pressure was reduced over time courses of several hours to as tong as 1 or 2 days.

4. The phrase, "Trandate Tablets therapy" has been changed to, "therapy with TRANDATE Tablets" throughout the text.

5. Under the PRECAUTIONS/Pediatric Use subsection, “children” has been changed to “pediatric patients.”

Your submission stated no later than November 17,1998 as the implementation date for the changes.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert dated June 1999). Accordingly, the supplemental application is approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.90 and 314.31.

If you have any questions, please contact:

Ms. Zelda McDonald
Regulatory Health Project Manager
(301) 594-5333

Sincerely yours,

Raymond J. Lipicky, M.D.
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